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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/981,998	05/11/98	PULST S	232.00010120

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EXAMINER	
GOLDBERG, J	
ART UNIT	**PAPER NUMBER**
1655	24

DATE MAILED: 11/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	08/981,998	PULST, STEFAN M.	
	Examiner	Art Unit	
	Jeanine A Enewold Goldberg	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *September 21, 2000; October 16, 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 59-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 59-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. The request filed on September 21, 2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/981,998 is acceptable and a CPA has been established. An action on the CPA follows.

2. Currently, claims 1-7, 59-61 are pending.

3. All previously pending and examined claims have been deleted in favor of new claims 1-7 and 59-61, thus all previous grounds of rejection are obviated.

4. This action contains new grounds of rejection.

Priority

5. Claims 1-3, 7, are given priority of 5/8/96. Claims 4-6, are given priority to the instant application, filing date of 5/11/98, because all of the claims contain SEQ ID NO: 4 and 5 which were first disclosed in the instant application. SEQ ID NO:s 1-3 were first disclosed in the parent application 08/727,084, filed 10/8/96. The priority to the 371 application also does not disclose the instant SEQ ID NO:s 4 and 5.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The essential elements of the claims are drawn to isolated nucleic acids encoding **any** mammalian SCA2 polypeptide wherein the isolated nucleic acid is either DNA or cDNA.

The specification teaches an isolated nucleic acid encoding the human SCA2 protein (pg. 6) and an isolated nucleic acid encoding the mouse SCA2 protein. The specification teaches SEQ ID NO: 1 and 2 which are the human nucleic acid and the corresponding polypeptide for SCA2, respectively. SEQ ID NO: 3 and 4 are the mouse nucleic acid and the corresponding polypeptide for SCA2, respectively. The specification teaches that the ataxin-2 related protein, A2RP, has a 42 amino acid domain which is 86% identical between the two proteins (pg. 11, 32, 47). A comparison of the human SCA2 gene to the mouse SCA2 gene indicates that the two sequences are only 88% identical. Further, the human SCA2 protein is 91% identical to the mouse SCA2 protein (see attachment).

There is not adequate description of the genus of nucleic acids encoding **any** mammalian SCA2 polypeptide wherein the isolated nucleic acid is either DNA or cDNA. Since it is known in the art that human and mouse genes are only 88% identical, the human and mouse SCA2 protein, SEQ ID NO: 3 and SEQ ID NO; 5 are only 91% identical and an ataxin-2 related protein has 86% identity to the SCA2 protein there is

unpredictability of the ability to detect SCA2 associated genes and proteins without detecting ataxin-2 related protein. Further, the identity of SCA2 between mammals may differ more than the difference of mouse and human and thus be less similar than the ataxin-2 related protein and would therefore detect ataxin-2 related protein more readily than the SCA2 associated gene or protein. Additionally, there is unpredictability in hybridization conditions which detect a SCA2 gene or protein without detecting the ataxin-2 related protein. The guidance in the specification only teaches two specific species of the large genus of mammalian SCA2 genes. There is no way to reasonably predict whether the mammalian genes in general are about 80-88% similar. In light of the 86% similarity of SCA2 protein to the ataxin-2 related protein, it is also unpredictable as to whether the human or mouse SCA2 would specifically hybridize to only SCA2 genes. The specification provides no guidance such as a zooblot to establish the specificity of the SCA2 gene for SCA2 genes in other mammals. Since the specification and the prior art do not provide any specific guidance to how to identify all mammalian SCA2 genes without identifying A2RP, the specification does not enable one skilled in the art to practice the invention without undue experimentation. The specification provides guidance about CAG repeat of SCA2 of SEQ ID NO: 1 and SEQ ID NO: 2. However, as written the claims are not clear that SCA2 is limited to SEQ ID NO: 1 or 2 or rather to any polypeptide which is associated with spinocerebellar ataxia type 2. There is variability among the species of nucleic acids encompassed in the scope of the claim as exemplified by the 86% similarity of the mouse and human. Furthermore, one of skill in the art would conclude that applicant was not in possession of the claimed

"nucleic acids encoding **any** mammalian SCA2 polypeptide wherein the isolated nucleic acid is either DNA or cDNA" because the description of only two members of this genus is not representative of the variants of the genus and is insufficient to support the claims. Thus, the specification does not adequately provide a written description for nucleic acids encoding **any** mammalian SCA2 polypeptide wherein the isolated nucleic acid is either DNA or cDNA.

7. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The essential elements of the claims are drawn to a DNA which encodes at least 10 contiguous amino acid residues of SEQ ID NO: 3 or 5.

The specification teaches an isolated nucleic acid encoding the human SCA2 protein (pg. 6) and an isolated nucleic acid encoding the mouse SCA2 protein. The specification teaches SEQ ID NO: 1 and 2 which are the human nucleic acid and the corresponding polypeptide for SCA2, respectively. SEQ ID NO: 3 and 4 are the mouse nucleic acid and the corresponding polypeptide for SCA2, respectively.
There is not adequate description of the genus of nucleic acids which are at least 10 contiguous amino acid residues which encode a mammalian SCA2 polypeptide. The specification only teaches the full length nucleic acid and amino acid sequence, however does not provide 30 mers which would encode a SCA2 polypeptide. The

general knowledge in the art concerning nucleic acids which are at least 10 contiguous amino acid residues does not provide any indication of how to readily identify these short sequences which encode SCA2. There is substantial variability among the species of nucleic acids encompassed in the scope of the claim. The specification has also not defined a structural feature of the nucleic acids which would be common to all members of the genus that constitutes a substantial portion of the genus. Furthermore, one of skill in the art would conclude that applicant was not in possession of the claimed "nucleic acid molecules which encode SCA2 which are 10 contiguous amino acids of SEQ ID NO: 3 or 5". Thus, the specification does not adequately provide a written description for "nucleic acid molecules which encode SCA2 which are 10 contiguous amino acids of SEQ ID NO: 3 or 5".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 5 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 5 is indefinite over the recitation "coding portion of the nucleotides 1-516 or SEQ ID NO: 1..." because it is unclear whether the claim is drawn to only the coding portion of nucleotides 1-516 of SEQ ID NO: 1 or whether the coding portion

limitation is also directed to nucleotides 163-4098 of SEQ ID NO:2, or nucleotides 50-3454 of SEQ ID NO: 4. Further, Claim 5 is indefinite over the recitation "coding portion of nucleotides.." because it is unclear whether all nucleotides between 163-4098 are coding nucleotides or whether there is a region within these nucleotides which are the coding nucleotides.

B) Claim 6 is indefinite over the recitation "substantially" because it is unclear to what extend substantially encompasses. Thus, the metes and bounds of the claimed invention are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-3, are rejected under 35 U.S.C. 102(b) as being anticipated by Gispert (Nature Genetics, 1993).

Gispert et al. (herein referred to as Gispert) teaches the chromosomal assignment of SCA2, cerebellar ataxia 2, to chromosome 12q23-24.1. Chromosome 12 has been isolated and analyzed (limitations of Claims 1-2). The claims as written broadly encompass the chromosome on which the SCA2 gene is located. Therefore

since Gispert teaches every limitation of the instant claims, Gispert reads on the claimed invention.

10. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Pulst et al. (Nature Genetics, 1993).

Pulst teaches the further localization of SCA2 to a 8.9 cM region, between IGF1 and D12S105/S84, with a maximum lod score of 3.6 (limitations of Claims 1-2). The claims as written broadly encompass the chromosome on which the SCA2 gene is located. Therefore since Pulst teaches every limitation of the instant claims, Pulst reads on the claimed invention.

11. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Imbert et al. (Nature Genetics, November 1996).

Imbert et al. (herein referred to as Imbert) teaches a polypeptide of 90 amino acids which is encoded by the nucleic acid of SEQ ID NO: 5. The nucleic acids from between 921-1190 of the instant application are 100% identical to the amino acids from 207-296 (limitations of Claim 4). Imbert teaches a nucleic acid sequences which is 99.8% identical to SEQ ID NO: 1 nucleotides 1-499 and thus would hybridize under high stringency conditions (limitations of Claim 5). Imbert teaches a nucleic acid sequence which is 88.1% identical (ie., substantially the same nucleotide sequence) to the nucleic acid sequence of SEQ ID NO: 2 with a best local similarity of 98.5% (limitations of Claim 6 and 10).

12. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Tora et al. (WO 97/17445).

Tora et al. (herein referred to as Tora) teaches a polypeptide of 90 amino acids which is encoded by for the nucleic acid of SEQ ID NO:5. The nucleic acids from between 921-1190 of the instant application are 100% identical to the amino acids from 207-296 (limitations of Claim 4). Tora further teaches a nucleic acid sequence which is 99.8% identical to nucleotides 10-499 of SEQ ID NO: 1 nucleotides 1-490 and thus would hybridized under high stringency conditions (limitations of Claim 5). Tora teaches a nucleic acid sequence which is 88.1% identical to the nucleic acid sequence of SEQ ID NO: 2 (limitations of Claim 6 and 10).

13. Claims 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (Genbank Accession Number, AA476524,January 1995).

Hillier teaches an amino acid sequences which matches 100% to the nucleic acid of SEQ ID NO: 3. The 172 contiguous amino acids are encoded by the nucleic acid of SEQ ID NO: 3 (limitations of Claim 4).

14. Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Ambrose et al. (Genbank Accession Number L27350, 1994).

Ambrose teaches 25 contiguous amino acids which are encoded by the nucleic acid sequence of SEQ ID NO:3.

15. Claims 5-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Pulst et al. (Nature Genetics, 1996).

Pulst et al. (herein referred to as Pulst) teaches a nucleic acid which is 99.8% identical to the nucleic acid sequence of SEQ ID NO: 1 nucleotides 1-499 and thus would hybridized under high stringency conditions (limitations of Claim 5). Pulst also teaches a mouse sequence which is 100% identical to the nucleic acid sequence of SEQ ID NO: 4 nucleotides 50-3454 and thus would hybridize under high stringency conditions (limitations of Claim 5). Pulst also teaches a nucleic acid sequence which is 100% identical to the nucleic acid sequence of SEQ ID NO: 2 (limitations of Claim 6 and 10). Pulst also teaches a nucleic acid sequence which is 77.9% identical to the sequence of SEQ ID NO: 4 (limitations of Claim 6). Oligonucleotides were end-labelled, FISH was performed and cDNA clones were isolated with P-labelled probes (pg. 275, col. 1)(limitations of Claim 11). Pulst teaches several different methods for identifying nucleic acids encoding SCA2 protein including FISH, and hybridization of (CAG)10 oligonucleotides followed by cloning and sequencing (pg. 275)(limitations of Claim 37). Pulst also teaches primers which were derived from SEQ ID NO: 2 and SEQ ID NO: 4 (pg. 275, para. 6).

16. Claims 6 and 59-61 are rejected under 35 U.S.C. 102(a) as being anticipated by Nechiporuk et al (Genbank Accession Number AF041472, January 1998).

Nechiporuk et al. (herein referred to as Nechiporuk) teaches a nucleic acid sequence which is 99.8% identical to the nucleic acid of SEQ ID NO: 4 (limitations of Claims 6 and 61). Nechiporuk teaches a nucleic acids encoding the amino acids sequence of SEQ ID NO: 5 (limitations of Claim 59). Nechiporuk teaches that the nucleic acid is a mouse homolog of the SCA2 gene (limitations of Claim 60).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gispert (Nature Genetics, July 1993) in view of Orr et al. (US. Pat 5,741,645, April 1998).

Gispert et al. (herein referred to as Gispert) teaches the chromosomal assignment of SCA2, cerebellar ataxia 2, to chromosome 12q23-24.1. Chromosome 12 has been isolated and analyzed (limitations of Claims 1-3).

Gispert does not specifically teach a vector or host cell containing the SCA2 nucleic acid.

However, Orr et al. (herein referred to as Orr) teaches a SCA1 gene which was isolated to the short arm of chromosome 6 (abstract). Orr also teaches that a gene probe is used for detecting the presence of a DNA sequence located within a SCA1 gene. The method includes digesting genomic DNA with restriction endonucleases to obtain DNA fragments, separating the fragments by size, probing the DNA fragments by size with a detestably labeled probe, and detecting the probe which hybridized to DNA fragments to analyze the DNA for (CAG)n regions characteristic of the normal or affected SCA1 gene (col. 2, lines 50-63)(limitations of Claim 37). Probes used for identifying DNA segments are labeled with radioactive or nonradioactive labels (col. 6, lines 20-43). Primers which hybridize to SCA1 genes on either side of the CAG repeat region, including directly adjacent to the CAG regions are disclosed (col. 3, lines 1-14)(limitations of Claim 40). Orr teaches a method of cloning a purified 1.2-kb fragment into a pBluescript plasmid (col. 10)(limitations of Claim 7).

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Gispert to include the teachings of Orr in order to make the invention. The ordinary artisan would have been motivated to insert the SCA2 gene into a vector and host cell, as taught by Orr, for the convenience of storing the gene and for the further cloning of the gene.

Conclusion

18. **No claims allowable.**

19. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Trottier et al. "Polyglutamine expansion as a pathological epitope in Huntington's disease and four dominant cerebellar ataxias", Nature, vol. 378, November 1995, p 403-406.

Trottier teaches that SCA2 is probably associated with CAG repeats, but the genes has not yet been identified.

B) Filla et al. "Has spinocerebellar ataxia type 2 a distinct phenotype?" Neurology, Vol. 45, April 1995, pg. 793-796.

Filla teaches clinical features of patients diagnosed with SCA2. Filla teaches only molecular genetic analysis may distinguish the different forms of SCA (pg. 796).

C) Sanpei et al. "Identification of the spinocerebellar ataxia type 2 gene using DIRECT" Nature Genetics, Nov 1996, pg. 277-284.

Sanpei teaches a method for detecting expansion of SCA2 CAG repeats using DIRECT. Probes and primers were disclosed to detect the SCA2 gene.

D) Lee, US Patent 5,853,995, December 29, 1998.

Lee teaches large scale genotyping of diseases and a diagnostic test for spinocerebellar ataxia type 6. Lee teaches a method for screening individuals at risk for developing diseases caused by trinucleotide repeat sequence instability by amplifying genomic DNA trinucleotide repeats

sequences in a sample from an individual to be tested by PCR using primers, labeling a probe capable of detecting the amplified DNA trinucleotide repeat sequences, comparing to a control, to determine whether the individual tested may be at risk for developing diseases caused by trinucleotide repeat sequences, if the DNA trinucleotide repeat sequence is larger than the control trinucleotide repeat sequence.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Enewold Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Thursday from 7:00AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Enewold Goldberg
November 15, 2000

Lisa B. Arthur

LISA B. ARTHUR
PRIMARY EXAMINER
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